# Low Anterior Resection Syndrome: Current Management and Future Directions

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### **Abstract**

Outcomes for rectal cancer surgery have improved significantly over the past 20 years with increasing rates of survival and recurrence, specifically local recurrence. These gains have been realized during a period of time in which there has been an increasing emphasis on sphincter preservation. As we have become increasingly aggressive in avoiding resection of the anus, we have begun accepting bowel dysfunction as a normal outcome. Low anterior resection syndrome, defined as a constellation of symptoms including incontinence, frequency, urgency, or feelings of incomplete emptying, has a significant impact on quality of life and results in many patients opting for a permanent colostomy to avoid these symptoms. In this article, we will highlight the most recent clinical and basic science research on this topic and discuss areas of future investigation.

# Keywords

- ► LAR syndrome
- ► rectal cancer
- ► low anterior resection

Oncologic outcomes for rectal adenocarcinoma have improved secondary to increased surveillance, improved chemotherapy, radiation, and surgical techniques. Low anterior resection (LAR) with total mesorectal excision (TME) for rectal cancer has allowed patients to avoid the permanent colostomy associated with abdominoperineal resection. As a result, an increasing number of patients are being managed with sphincter-sparing surgery. In general, surgeons assume that patients would like to avoid a permanent colostomy, and patients likely assume that in preserving their sphincter, their bowel function will not change significantly following rectal resection, or effects will be short term. However, more and more data suggest that a large majority (up to 90%) of patients experience long-term changes in quality of life from symptoms following LAR.<sup>2</sup> Recently published data from a multicenter European consortium collected information on patients' symptoms and quality of life following LAR. They showed a correlation between decreasing quality of life scales and high LAR syndrome score. In this study, the symptom most associated with low quality of life was diarrhea.<sup>3</sup>

LAR syndrome is difficult to define. Patients may have a combination of symptoms including frequency, urgency, incontinence, and constipation which may last longer than an initial adaptive period.<sup>4</sup> Patients typically fall into two

categories: those with incontinence, frequency, and urgency, and those with constipation and feelings of incomplete emptying, but some patients report features of both, either occurring simultaneously or vacillating between these two constellations of symptoms. This review focuses on the background of LAR syndrome, pathophysiologic features of LAR syndrome, surgical reconstruction options to reduce LAR syndrome, and current research within the field of postoperative bowel dysfunction.

#### Pathophysiology of LAR Syndrome

LAR syndrome is likely multifactorial. Many potential pathophysiologic mechanisms for LAR syndrome have been proposed: internal anal sphincter (IAS) dysfunction, decrease in anal canal sensation, disappearance of the rectoanal inhibitory reflex (RAIR), disruption in local reflexes between the anus and the neorectum, and reduction in rectal reservoir capacity and compliance all have been described.

#### **Internal Anal Sphincter Dysfunction**

Pelvic surgery carries a risk of injury to many structures, including the IAS. Anatomic studies have shown that sympathetic nerves supplying the IAS course intersphincterically,

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and as a result are likely to be injured in LAR for rectal cancer, affecting function.<sup>5</sup> Differences in IAS pressure before and after surgery are likely to contribute to LAR syndrome. In a 21-patient cohort, preoperative and postoperative resting IAS pressures were measured in patients undergoing LAR, and those with low resting pressures frequently exhibited incontinence. In addition, this study showed a correlation between length of the remaining rectum and ratio of the decrease in maximum resting pressure (postoperative/preoperative maximum resting pressure), suggesting that the lower the resection, the more incontinence patients exhibit. 6 IAS injury has been observed radiographically with rectal ultrasound following stapled LAR for rectal cancer. In a 1998 study, 39 patients with rectal cancer were examined endosonographically for signs of IAS injury (most commonly a thinned IAS), both before and after LAR. No preoperative IAS defects were observed, and following LAR, a total of seven patients were found to have IAS defects after a 2-year follow-up.<sup>7</sup> These studies suggest that parasympathetic nerve damage and/or surgical IAS damage is associated with reduced IAS function and LAR syndrome.

#### **Decrease in Anal Canal Sensation**

Like IAS dysfunction, decreased anal canal sensation may be related to nervous damage during LAR. In a 232-patient series, the ability to differentiate flatus from feces has been associated with increased anal verge-anastomotic distance.8 Studies have sought to quantitatively examine anal mucosal electrosensitivity in preoperative and postoperative LAR patients. One such study demonstrated differences in preoperative sensitivity thresholds between patients with and without postoperative fecal incontinence, but significance was not demonstrated.<sup>9</sup> Another divided two groups of patients who have undergone LAR into those with and without incontinence, and demonstrated lower anal canal sensitivity at the dentate line in patients with incontinence, which was statistically significant. 10 These studies demonstrate that anal canal sensitivity may be decreased, but the evidence is mixed.

# Disappearance of the Rectoanal Inhibitory Reflex and Communication between the Anus and the Neorectum

The RAIR is described as transient relaxation of the IAS in response to rectal dilation. It has been suggested that via a "sampling mechanism," the upper anal canal discriminates between flatus and feces, and that rectal dilation relaxes the IAS via nitric oxide pathways. 11 The RAIR has been studied in preoperative and postoperative patients with symptoms of LAR syndrome. One such study of patients with and without satisfactory defecatory function (defined by Wexner continence questionnaire) was assessed with anorectal manometry and balloon proctometry. RAIR, maximum threshold volume on balloon proctometry, and length of the high pressure zone on manometry were shown to be independent predictors of poor 12-month function after LAR. 12 These results have been reproduced in patients with varying lengths of remaining rectum, with better functional outcomes in those patients with > 4 cm of remaining rectum. 13 Furthermore, research on

RAIR in patients undergoing ileal pouch-anal anastomosis (IPAA) after proctocolectomy for ulcerative colitis (UC) has shown correlation between preservation of the RAIR and decreases in the incidence of incontinence.<sup>14</sup> The function of the RAIR seems to be pivotal to function, and loss of the RAIR after LAR is supported by the literature.

#### **Reduction in Rectal Reservoir Capacity and Compliance**

The rectum has an inherent reservoir capacity and compliance which allows for proper storage of stool before evacuation. With proper TME, only a few centimeters of rectum above the dentate line remain, leaving little reserve and compliance function. As a result, the little rectum left after TME likely does not contribute significantly to capacity and compliance. This has been demonstrated in patients undergoing colectomy, mucosal proctectomy, and endorectal IPAA for UC and familial polyposis, showing greater slope in pressure-volume curves and decreased maximum capacity following surgery compared with controls. In addition, they showed that a greater capacity of the neorectum was associated with a significant functional decrease in the number of bowel movements/day.<sup>15</sup> A large portion of data on capacity and compliance originates from Europe. In a study of 35 consecutive Norwegian patients undergoing LAR, rectal volume eliciting urge to defecate and maximum tolerable rectal volume were significantly reduced after operation. Distance of the rectal remnant was also measured, and maximum tolerable volume was lower in patients with a low anastomosis compared with a high anastomosis. 16 Data in LAR patients also shows via balloon proctometry a reduction in rectal capacity and compliance which slowly recovered to close to preoperative levels, but only after a year following surgery. 13 Radiation therapy (RT) may contribute in part to functional outcomes following TME. Data in a 2002 Dutch study showed that RT + TME was associated with higher frequency of defecation compared with TME alone, and compliance was significantly reduced after RT + TEM at 4 and 12 months, respectively.

# Surgical Reconstruction Techniques to Reduce LAR Syndrome

The reduction in capacity and compliance following TME in patients with straight coloanal anastomosis (SCAA) has led to several surgical techniques to account for this change in the neorectum. Side-to-end coloanal anastomoses, colonic J-pouch-anal anastomoses (CJPAAs), and transverse coloplasty pouch (TCP) have been performed and studied. This section will describe the technique for construction of these neorectal reservoirs and discuss the various benefits of each of these methods.

#### **Straight Coloanal Anastomosis**

The most common coloanal anastomotic technique is the SCAA. During the anterior resection, the distal resection margin is typically removed with a straight stapler. As with any anastomosis, care should be taken to ensure the new coloanal anastomosis retains proper blood supply and is not

under tension in the pelvis. Performing the anastomosis typically utilizes a circular intraluminal stapler with an anvil mechanism. The proximal resection margin is attached to the anvil in a purse-string fashion. Then, the circular stapler is inserted into the rectum through the anus, and the spike of the intraluminal stapler is carefully extended and penetrated through the stapled distal margin, in the middle of the staple line. The anvil is then attached to the spike, ensuring the bowel is appropriately aligned and not twisted. The stapler is carefully closed and fired. The stapler is carefully removed, and the anastomotic "donut" is examined to ensure a good circular staple all around the anastomosis.

As mentioned previously, much of the background for LAR syndrome came from concern for pathophysiology of compliance and capacity of the SCAA. As the oldest and first technique for low rectal anastomosis, subsequent studies of neorectal reconstruction techniques have focused on comparisons to SCAA. In practice, SCAA is used when length limitations on the proximal bowel exist or the pelvis is too narrow and not accepting of a J-pouch, coloplasty, or side-to-end anastomosis.

#### **Colonic J-Pouch-Anal Anastomosis**

In an effort to combat some of the concerns about poor neorectal compliance and capacity of the SCAA technique, the colonic J-pouch-anal anastomosis was developed. Original publications on CJPAA were performed with large pouches, 10 to 12 cm and up to 15 cm in length. 17 Constructing a CJPAA typically requires full mobilization of the splenic flexure and ligation of the inferior mesenteric artery and the left colic artery at their origins, and the inferior mesenteric vein at the inferior edge of the pancreas. This allows the left colon to straighten out so that there is sufficient length of bowel to both construct the pouch and to then have it go easily, and without tension, to the anus. In constructing the pouch, the distal sigmoid or the descending colon is folded so that the colonic side walls touch. A colostomy is made just lateral to the antimesenteric border at the corner of the fold, and a linear stapler is fed intraluminally through the colotomy to either side of the colonic side walls and fired. The anvil of a circular stapler is then secured with a purse string at the colotomy, or marking sutures are placed at the colotomy if a transanal handsewn anastomosis is to be constructed. The pouch is taken to the pelvis with the mesentery posterior and the tip of the I to the right. Concerns about the optimal length of the pouch developed from variability in pouch size cited in the literature along with some patients reporting symptoms of incomplete emptying of the pouch. When 6 and 10 cm pouch lengths were compared in a randomized prospective study, patients with smaller pouch sizes described less laxative and/or enema use for evacuation.

Lazorthes et al described this technique in 1986. Their case series described 65 patients with rectal cancer, 20 of which had construction of a CJPAA. During the first year, 60% of patients described having one to two bowel movements/day during the first year, compared with 33% with SCAA. After the first year, 86% of pouch patients and 33% of SCAA patients described one to two bowel movements/day. In addition, the

maximum tolerated volume of the neorectum was greater with the pouch, and those patients who described themselves as having "normal continence" was 60% with the pouch versus 42% without. The Several prospective randomized studies have been done comparing CJPAA and SCAA. In 1995, Seow-Choen and Goh concluded improved defecatory function with CJPAA, with all patients in their CJPAA cohort describing normal continence at < 3 bowel movements/day. Additional trials have supported 1-year follow-up defecatory function, with less bowel movement frequency and urgency and better continence for CJPAA patients. Hallböök et al even reported a lower anastomotic leak rate of 2% in 47 CJPAA patients versus 15% for 42 patients receiving SCAA.

Longer term follow-up of CJPAA and SCAA has been performed as well. Following a total of 42 consecutive patients randomized to either CJPAA or SCAA, Ho et al showed no difference in defecatory function, including no difference in soiling with flatus or frequency at 2 years, though short-term outcomes at 6 months were still improved in CJPAA patients. In a 1998 study of 173 patients contacted via telephone follow-up at a mean of 5 years, patients with a CJPAA had significantly better frequency, clustering, and were less likely to have to adhere to a restricted diet or use constipating agents to maintain function, suggesting that CJPAA may be the best long-term option for TME following rectal cancer. In the constitution of the constitutio

#### **Side-to-End Anal Anastomosis**

The side-to-end anal anastomosis (SEAA) was originally described in 1950 by Baker.<sup>24</sup> Originally described using a handsewn technique, SEAA is now typically performed with the conventional intraluminal stapler through the anus, with the anvil placed through a colotomy on the antimesenteric side of the colon and purse string sutured in place. Some surgeons will leave a several (3–4) centimeters blind end when performing a SEAA, but examination of effectiveness of this technique has not been shown in the literature.

In the 1990s, initial recognition of LAR syndrome and the choice of the best anastomotic technique resulted in several trials examining SEAA as an option to improve long-term bowel function after anterior resection. Huber et al performed the first prospective randomized trial of SEAA to CJPAA. Patients underwent preoperative evaluation and had 3- and 6-month follow-up evaluations. During the follow-up period, SEAA patients had higher stool frequency at 3 months, but at 6 months, frequency was nearly identical. Similar postoperative complications, anal manometry, and constipation were seen in both groups, though CJPAA patients did demonstrate higher maximum tolerated volume and threshold volume.<sup>25</sup> Machado et al in 2003 described a prospective series of 100 patients randomized to either SEAA or CIPAA (50 in each group), and performed 6- and 12-month evaluation. The techniques were not different in preoperative demographics, operative factors, or immediate postoperative outcomes. Combined functional rank scores were similar between the two groups, and most functional outcomes examined were similar between the groups, concluding that SEAA and CJPAA seemed equivalent.<sup>26</sup> Using the same patients, the study group was followed up out to 2 years, also showing no statistical difference in functional outcomes, though pouch patients exhibited approximately 40% greater neorectal volume and higher compliance.<sup>27</sup> In a similar study of 56 patients, Jiang et al examined CJPAA versus SEAA technique being performed transabdominally. The study showed similar functional outcomes out to 2 years in SEAA and CJPAA patients, though CJPAA patients appeared to "recover" bowel function faster at 6 and 12 months compared with SEAA.<sup>28</sup> As with the previous studies, they concluded SEAA as equivalent to CJPAA for reconstruction after LAR.

#### **Transverse Coloplasty Pouch**

The TCP neoreservoir was first described in 1999 by a Swiss colorectal group as an alternative to the SCAA and CJPAA. In a pig model, the study observed less volume with TCP as compared with CJPAA, and TCP was easier to perform and took less time, and qualitative observations on postoperative bowel function of TCP pigs claimed improved consistency and decreased urgency compared with SCAA and less incomplete evacuation compared with CJPAA.<sup>29</sup> The same Swiss group first described the technique of constructing a TCP in humans. The specimen is resected in typical fashion, and the distal end of the remaining colon is used to make the coloplasty. The distal end of the colon is attached to the anvil of an intraluminal stapler in a purse-string manner. Then, a 7- to 9-cm longitudinal incision is made on the antimesenteric side of the distal colon, starting at least 2 cm from the rim of the anvil (many studies quote 3-4 cm from the stapled edge). The antimesenteric incision is then closed transversely with a single layer of seromuscular absorbable sutures. The intraluminal stapler is inserted into the anus, the pouch is placed in the pelvis, and the stapler fired in the usual fashion.<sup>30</sup>

Short-term follow-up of patients undergoing TCP by the Swiss group demonstrated the safety of TCP with a 7% anastomotic leak rate, and similar 6- and 8-month followup bowel dysfunction, though this was not directly compared with SCAA, SEAA, or CJPAA.<sup>31</sup> As TCP was developed as a safe alternative to CJPAA, three randomized trials have been performed comparing the two techniques. The first and largest of these three performed from 1998 to 2000 in Singapore followed 88 patients randomized to either CJPAA or TCP. CJPAA was performed using a 6-cm pouch, and TCP was performed with a 7-cm incision made 4 cm proximal to the cut end. Patients were followed for immediate postoperative complications and 4- and 12-month bowel function follow-up. TCP patients had a higher rate of anastomotic leak (15.9 vs. 0%), several of which required intervention. During follow-up, TCP patients exhibited better deferral of bowel movements and less nocturnal leakage, but more stool fragmentation at 4 months, but no differences in bowel function among 12 parameters were observed at 1 year. Quality of life scoring was also performed and showed no difference between the groups.<sup>32</sup>

In response to the claims that TCP improves continence due to a decrease colonic motility, Fürst et al, using comparable surgical methods, compared 40 patients randomized to CJPAA or TCP. In 25% of patients, CJPAA was unable to be performed due to technical limitations. Immediate postoperative complications were not different, and functional outcomes were assessed at 6 months postoperatively. Though postoperative neorectal threshold volume was higher in the CJPAA group, no differences in bowel function (frequency, continence to gas and liquids, urgency, clustering, or straining) were observed during the follow-up period.<sup>33</sup> Finally, 30 Portuguese patients were randomized to CJPAA or TCP with similar postoperative complications, as well as postoperative bowel function indices at 3-, 6-, and 12-month intervals, though the study does mention two patients in the CJPAA group having to use enemas for complete evacuation. Manometry data were similar between the two groups.<sup>34</sup>

#### Comparing SCAA, CJPAA, and TCP Techniques

In an effort to compare postoperative complications, functional outcomes, and quality of life of three of these techniques (SCAA, CJPAA, and TCP), a multicenter randomized trial of 364 patients over 4 years was performed by Fazio et al. After oncologic resection, patients were deemed either eligible or ineligible for CJPAA based on the ability of the operating surgeon to reliably construct a 5-cm J-pouch. If deemed eligible, patients were randomized to CJPAA or TCP. In the case where CJPAA was not technically feasible, patients were randomized to receive either SCAA or TCP. Immediate postoperative complications and 4-,12-, and 24-month follow-up were examined. The study reported similar demographics among the four groups, but when comparing the J-pouch eligible and ineligible groups, the ineligible group had a significantly higher body mass index. No differences in immediate postoperative complications were observed among the four groups. In the J-pouch ineligible arm, the study did not find any significant differences in bowel movements, urgency, pad usage, clustering, and medication usage for bowel dysfunction between SCAA and TCP. However, in the J-pouch eligible arm, the authors found significant differences in total daily bowel movements, fecal incontinence severity index, and clustering in favor of CJPAA over TCP. Quality of life measures did not show any significance among the groups. As a result of these data, the study concluded that in patients where CJPAA is feasible, it should be performed, but in those patients where J-pouch creation is not technically feasible, there seems to be no difference between TCP and SCAA.<sup>35</sup>

#### Research and Treatments for LAR Syndrome

Much research has shown that the pathophysiology of LAR syndrome seems to be intimately related to neorectal compliance and capacity, and research on surgical techniques to improve these parameters, particularly with the success of the J-pouch as a functional improvement has supported this hypothesis. However, little attention has been focused on the autonomic innervation of the colon and rectum, the differences in motility patterns that exist between the colon and rectum, and how, functionally, the colon and rectum rely on sympathetic and parasympathetic function to varying degrees.

Involuntary control of the distal colon and rectum is regulated by the autonomic nervous system and enteric nervous system. The autonomic nervous system is further characterized by parasympathetic and sympathetic components. During the course of a standard resection for rectal cancer both the sympathetic and parasympathetic fibers to the distal colon, which will become the neorectum, are transected. This leaves the neorectum under the control of the enteric nervous system. Taking the inferior mesenteric artery (IMA) and the left colic arteries at their origin disrupts the sympathetic autonomic nerves that travel with these vessels. The parasympathetic input of the neorectum comes at least partially from the pelvis, and during rectal dissection, this innervation is disrupted. Therefore, the neorectum, whether constructed as a SCAA, SEAA, TCP, or CJPAA, will exist as a segment of bowel that has, at least partially, been extrinsically denervated, and this will affect how the remaining bowel behaves functionally.

It is very likely that much of what is recognized as LAR syndrome is actually related to what happens to the autonomic innervation of the neorectum during the course of the extensive mobilization that occurs during a LAR. The authors have observed in the operating room that after the complete mobilization and division of bowel required as part of a LAR (in preparation for a coloanal anastomosis), there are very strong contractions that randomly take place in the distal transverse and descending colon: they never start or progress into the mid- or proximal transverse colon. We have hypothesized that the disordered bowel function, known as LAR syndrome, is a result of motility changes seen in the left colon following extrinsic denervation that occurs with the extensive mobilization performed during these operations.

Furthermore, in an animal model, the authors have investigated motility patterns of the left colon after extrinsic denervation.<sup>36</sup> The results of this study suggest that surgical denervation of descending colon, which is frequently performed as part of distal colon and LAR operations to obtain a tension-free anastomosis, can change the motility of the left colon. In support of this concept, there are data suggesting that neorectal reservoir is not the functional principle of the colonic J-pouch and that "the major functional principle of the colonic J-pouch is predominantly related to delayed propulsive motility."37 The two currently available reconstructive techniques used to reduce symptoms of the LAR syndrome, colonic J-pouch, and transverse coloplasty pouch, may succeed based on the fact that both interrupt the strong contractions seen in the left colon as a result of denervation. This remains to be proven.

Based on the hypothesis that LAR syndrome is at least partially a result of extrinsic denervation of the descending colon/neorectum, further animal studies have shown that rectal motility relies much more on parasympathetic activity and is inhibited by sympathetic activity  $^{38}$  but recovers over time.  $^{39}$  In response to adrenergic blockade, colonic motility increases in animal models, suggesting the sympathetic nervous system tonically inhibits colon motility.  $^{40}$  Furthermore, this extrinsic innervation seems to affect propagation time, slowing and controlling it rhythmically through  $\alpha$ -adrenergic mechanisms.  $^{36,41}$ 

Further research on receptor-mediated colonic transit has shown specific subtypes of serotonin receptors seem to have a role in regulation of colonic motility after denervation. The enteric nervous system is composed of two major interconnected plexuses of ganglia and nerve processes, the myenteric plexus and the submucosal plexus. Intrinsic primary afferent neurons (IPANs) have cell bodies in the myenteric plexus or in the submucosal plexus and processes extending to muscularis mucosa as well as processes synapsing with interneurons. IPANs are the primary sensors and regulators of the enteric nervous system via serotonin receptors.

Serotonin is a neurotransmitter of profound importance in the enteric nervous system. About 95% of the serotonin in the body are found in the GI tract. It plays a key role in the initiation of peristaltic and secretory reflexes. Although more than 25 different types of serotonin (5-HT) receptors exist, 5-HT3 and 5-HT4 receptors play important roles in peristaltic reflexes. Following pelvic parasympathetic denervation, serotonin receptors upregulate within several weeks in rat models in an effort to restore normal colonic function. With the knowledge that serotonin antagonists can be useful in nonsurgical disorders of GI motility, a ramosetron, a serotonin receptor antagonist was given to patients with symptoms of urgency and incontinence following LAR with significant improvement in urgency and bowel movements per day.

Implantable sacral nerve stimulators (SNSs) have been studied in patients with medically refractory incontinence. Through a minor surgical procedure, electrodes can be inserted into the S2-S4 sacral foramen and connected to a subcutaneous pulse generator. One large prospective trial has shown very promising results of these devices for medically refractory fecal incontinence, with significant decreases in incontinent episodes and acceptable safety. Further follow-up using the same patient population has even shown improvement in quality of life scoring with the device. Although this study specifically excluded patients with prior rectal surgery, the study shows improvement in fecal incontinence in patients with sphincter trauma, suggesting these devices could provide some utility for patients with LAR syndrome. The ultimate mechanism by which SNS is effective is largely unknown.

Biofeedback therapy (BFT), the process by which patients are trained with myometry and balloons to strain effectively and relax the sphincter, has met with some success in patients with bowel outlet dysfunction.<sup>51</sup> Byrne et al published a retrospective review of 513 patients undergoing BFT, 13% of which had prior rectal surgery. The study reported significant improvement in incontinence, sphincter pressures, and quality of life following therapy, with completion of all six treatment sessions being associated with a 10x greater odds ratio of success.<sup>52</sup> Although successful, the majority of patients in this study were women with history of vaginal delivery, vaginal tear, and/or hysterectomy or other pelvic floor surgery. A prospective study of 13 patients (7 of which underwent LAR) demonstrated reduction in stool frequency, incontinence episodes, and antidiarrheal agent usage following BFT.<sup>53</sup> Furthermore, in a retrospective review of 70 patients with anterior resection syndrome who underwent BFT, fecal incontinence scores, number of bowel movements/day, use of antidiarrheal medications, and rectal capacity improved significantly following BFT.<sup>54</sup> In a similar study, 19 patients receiving BFT following surgical colorectal resection showed improved continence, decreased bowel movements/day, and even increased quality of life.<sup>55</sup> Although most of this research has occurred in small sample sizes or through retrospective review, BFT remains a fairly noninvasive and successful method for treating anterior resection syndrome.

#### **Discussion**

LAR syndrome is a significant problem facing a large percentage of patients after surgical resection for rectal cancer. Characterized by a constellation of symptoms ranging from incontinence with frequency and urgency to constipation and incomplete emptying, LAR syndrome has the potential to affect quality of life in this patient population. Like the symptom profile, the pathophysiology of LAR syndrome is difficult to define and is likely related to a multifactorial process including IAS dysfunction and/or injury, decreases in anal canal sensation, changes in the rectoanal inhibitor reflex, and reduction in rectal reservoir capacity and compliance.

Several surgical options for neorectal construction exist, each with their own purported benefits and anatomic and physiologic rationale. This review of the literature seems to support the use of a short 5 to 6 cm CJPAA as the best immediate and long-term option for bowel function. Some studies show TCP and SEAA to be equivalent to CJPAA, but no studies exist comparing TCP and SEAA to SCAA. Of the one study, this review found TCP compared with SCAA had no significant improvement in bowel function parameters. In addition, one study showed a significantly higher rate of anastomotic leak in patients undergoing TCP compared with CJPAA. However, this study reported a 0% leak rate in CJPAA patients, so differences could be related to experienced construction of CJPAA compared with a potential learning curve with construction of a TCP. A Cochrane review of reconstruction techniques after rectal resection was published in 2008. The authors conclude essentially three points based on studies reviewed: (1) CJPAA is superior to SCAA, (2) SEAA and TCP appear equivalent to CJPAA in small prospective randomized controlled trials, but limited data support SEAA and TCP over SCAA, and (3) further study is needed to determine the role of alternative anastomotic strategies. This review of the literature supports the findings of the Cochrane study.

Research into LAR syndrome seems to point to compliance and capacity as primary pathophysiologic factors. However, several other mechanisms including loss of extrinsic nervous signals with colonic dissection and serotonin receptor upregulation seem to play a role in LAR syndrome. SNS may be a treatment option for those with LAR syndrome predominated by fecal incontinence. Although the majority of the literature on biofeedback has been performed in patients with pelvic floor dysfunction, BFT may play a role in LAR syndrome, especially as a noninvasive, nonmedicinal option with long-lasting results.

In conclusion, LAR syndrome is difficult to define with a large range of symptoms supported in the literature. As has

been suggested in the literature, long-term follow-up with standardized questionnaires for bowel, bladder, and sexual function and quality of life would elucidate the definition. The best surgical reconstruction option appears to be CJPAA if feasible, with SCAA, SEAA, and TCP as options when CJPAA is not technically feasible. Finally, more research on the basic science behind colonic motility, feedback mechanisms, and compensatory factors would prove useful for eventual development of novel techniques to treat LAR syndrome.

#### References

- 1 Monson JR, Weiser MR, Buie WD, et al; Standards Practice Task Force of the American Society of Colon and Rectal Surgeons. Practice parameters for the management of rectal cancer (revised). Dis Colon Rectum 2013;56(5):535–550
- 2 Dennett ER, Parry BR. Misconceptions about the colonic J-pouch: what the accumulating data show. Dis Colon Rectum 1999;42(6): 804–811
- 3 Juul T, Ahlberg M, Biondo S, et al. Low anterior resection syndrome and quality of life: an international multicenter study. Dis Colon Rectum 2014;57(5):585–591
- 4 Bryant CL, Lunniss PJ, Knowles CH, Thaha MA, Chan CL. Anterior resection syndrome. Lancet Oncol 2012;13(9):e403–e408
- 5 Ishiyama G, Hinata N, Kinugasa Y, Murakami G, Fujimiya M. Nerves supplying the internal anal sphincter: an immunohistochemical study using donated elderly cadavers. Surg Radiol Anat 2014; 36(10):1033-1042
- 6 Williamson ME, Lewis WG, Holdsworth PJ, Finan PJ, Johnston D. Decrease in the anorectal pressure gradient after low anterior resection of the rectum. A study using continuous ambulatory manometry. Dis Colon Rectum 1994;37(12):1228–1231
- 7 Farouk R, Duthie GS, Lee PW, Monson JR. Endosonographic evidence of injury to the internal anal sphincter after low anterior resection: long-term follow-up. Dis Colon Rectum 1998;41(7): 888–891
- 8 Karanjia ND, Schache DJ, Heald RJ. Function of the distal rectum after low anterior resection for carcinoma. Br J Surg 1992;79(2): 114–116
- 9 Komatsu J, Oya M, Ishikawa H. Quantitative assessment of anal canal sensation in patients undergoing low anterior resection for rectal cancer. Surg Today 1995;25(10):867–873
- Tomita R, Igarashi S, Fujisaki S. Studies on anal canal sensitivity in patients with or without soiling after low anterior resection for lower rectal cancer. Hepatogastroenterology 2008;55(85): 1311–1314
- 11 Kaur G, Gardiner A, Duthie GS. Rectoanal reflex parameters in incontinence and constipation. Dis Colon Rectum 2002;45(7): 928–933
- 12 Kakodkar R, Gupta S, Nundy S. Low anterior resection with total mesorectal excision for rectal cancer: functional assessment and factors affecting outcome. Colorectal Dis 2006;8(8):650–656
- 13 Lee SJ, Park YS. Serial evaluation of anorectal function following low anterior resection of the rectum. Int J Colorectal Dis 1998; 13(5-6):241-246
- 14 Saigusa N, Belin BM, Choi HJ, et al. Recovery of the rectoanal inhibitory reflex after restorative proctocolectomy: does it correlate with nocturnal continence? Dis Colon Rectum 2003;46(2): 168–172
- 15 Heppell J, Kelly KA, Phillips SF, Beart RW Jr, Telander RL, Perrault J. Physiologic aspects of continence after colectomy, mucosal proctectomy, and endorectal ileo-anal anastomosis. Ann Surg 1982; 195(4):435–443
- 16 Nesbakken A, Nygaard K, Lunde OC. Mesorectal excision for rectal cancer: functional outcome after low anterior resection and

- colorectal anastomosis without a reservoir. Colorectal Dis 2002; 4(3):172-176
- 17 Lazorthes F, Fages P, Chiotasso P, Lemozy J, Bloom E. Resection of the rectum with construction of a colonic reservoir and colo-anal anastomosis for carcinoma of the rectum. Br J Surg 1986;73(2):136-138
- 18 Seow-Choen F, Goh HS. Prospective randomized trial comparing J colonic pouch-anal anastomosis and straight coloanal reconstruction. Br J Surg 1995;82(5):608-610
- 19 Ortiz H, De Miguel M, Armendáriz P, Rodriguez J, Chocarro C. Coloanal anastomosis: are functional results better with a pouch? Dis Colon Rectum 1995;38(4):375-377
- 20 Hallböök O, Påhlman L, Krog M, Wexner SD, Sjödahl R. Randomized comparison of straight and colonic J pouch anastomosis after low anterior resection. Ann Surg 1996;224(1):58-65
- 21 Lazorthes F, Chiotasso P, Gamagami RA, Istvan G, Chevreau P. Late clinical outcome in a randomized prospective comparison of colonic I pouch and straight coloanal anastomosis. Br I Surg 1997;84(10):1449-1451
- 22 Ho YH, Seow-Choen F, Tan M. Colonic J-pouch function at six months versus straight coloanal anastomosis at two years: randomized controlled trial. World J Surg 2001;25(7):876–881
- 23 Dehni N, Tiret E, Singland JD, et al. Long-term functional outcome after low anterior resection: comparison of low colorectal anastomosis and colonic J-pouch-anal anastomosis. Dis Colon Rectum 1998;41(7):817-822, discussion 822-823
- 24 Baker JW. Low end to side rectosigmoidal anastomosis; description of technic. Arch Surg 1950;61(1):143-157
- 25 Huber FT, Herter B, Siewert JR. Colonic pouch vs. side-to-end anastomosis in low anterior resection. Dis Colon Rectum 1999;
- 26 Machado M, Nygren J, Goldman S, Ljungqvist O. Similar outcome after colonic pouch and side-to-end anastomosis in low anterior resection for rectal cancer: a prospective randomized trial. Ann Surg 2003;238(2):214-220
- 27 Machado M, Nygren J, Goldman S, Ljungqvist O. Functional and physiologic assessment of the colonic reservoir or side-to-end anastomosis after low anterior resection for rectal cancer: a twoyear follow-up. Dis Colon Rectum 2005;48(1):29-36
- 28 Jiang JK, Yang SH, Lin JK. Transabdominal anastomosis after low anterior resection: a prospective, randomized, controlled trial comparing long-term results between side-to-end anastomosis and colonic J-pouch. Dis Colon Rectum 2005;48(11):2100-2108, discussion 2108-2110
- $\,$  29  $\,$  Z'graggen K, Maurer CA, Mettler D, Stoupis C, Wildi S, Büchler MW. A novel colon pouch and its comparison with a straight coloanal and colon J-pouch—anal anastomosis: preliminary results in pigs. Surgery 1999;125(1):105-112
- 30 Z'graggen K, Maurer CA, Büchler MW. Transverse coloplasty pouch. A novel neorectal reservoir. Dig Surg 1999;16(5):363-366
- 31 Z'graggen K, Maurer CA, Birrer S, Giachino D, Kern B, Büchler MW. A new surgical concept for rectal replacement after low anterior resection: the transverse coloplasty pouch. Ann Surg 2001;234(6): 780-785, discussion 785-787
- 32 Ho YH, Brown S, Heah SM, et al. Comparison of J-pouch and coloplasty pouch for low rectal cancers: a randomized, controlled trial investigating functional results and comparative anastomotic leak rates. Ann Surg 2002;236(1):49-55
- 33 Fürst A, Suttner S, Agha A, Beham A, Jauch KW. Colonic J-pouch vs. coloplasty following resection of distal rectal cancer: early results of a prospective, randomized, pilot study. Dis Colon Rectum 2003; 46(9):1161-1166
- 34 Pimentel JM, Duarte A, Gregório C, Souto P, Patrício J. Transverse coloplasty pouch and colonic J-pouch for rectal cancer-a comparative study. Colorectal Dis 2003;5(5):465-470
- 35 Fazio VW, Zutshi M, Remzi FH, et al. A randomized multicenter trial to compare long-term functional outcome, quality of life, and complications of surgical procedures for low rectal cancers. Ann Surg 2007;246(3):481-488, discussion 488-490

- 36 Lee WY, Takahashi T, Pappas T, Mantyh CR, Ludwig KA, Surgical autonomic denervation results in altered colonic motility: an explanation for low anterior resection syndrome? Surgery 2008; 143(6):778-783
- 37 Fürst A, Burghofer K, Hutzel L, Jauch KW. Neorectal reservoir is not the functional principle of the colonic J-pouch: the volume of a short colonic J-pouch does not differ from a straight coloanal anastomosis. Dis Colon Rectum 2002;45(5):660-667
- 38 Ridolfi TJ, Tong WD, Takahashi T, Kosinski L, Ludwig KA. Sympathetic and parasympathetic regulation of rectal motility in rats. J Gastrointest Surg 2009;13(11):2027–2033, discussion 2033
- 39 Ridolfi TJ, Tong WD, Kosinski L, Takahashi T, Ludwig KA. Recovery of colonic transit following extrinsic nerve damage in rats. Scand J Gastroenterol 2011;46(6):678-683
- 40 Gillis RA, Dias Souza J, Hicks KA, et al. Inhibitory control of proximal colonic motility by the sympathetic nervous system. Am J Physiol 1987;253(4 Pt 1):G531-G539
- 41 Tanabe Y, Hotokezaka M, Mibu R, Tanaka M. Effects of extrinsic autonomic denervation and myenteric plexus transection on colonic motility in conscious dogs. Surgery 2002;132(3):471-479
- 42 Costedio MM, Hyman N, Mawe GM. Serotonin and its role in colonic function and in gastrointestinal disorders. Dis Colon Rectum 2007;50(3):376-388
- 43 Gershon MD, Tack J. The serotonin signaling system: from basic understanding to drug development for functional GI disorders. Gastroenterology 2007;132(1):397-414
- Grider JR, Foxx-Orenstein AE, Jin JG. 5-Hydroxytryptamine4 receptor agonists initiate the peristaltic reflex in human, rat, and guinea pig intestine. Gastroenterology 1998;115(2):
- 45 Tong W, Kamiyama Y, Ridolfi TJ, et al. The role of 5-HT3 and 5-HT4 receptors in the adaptive mechanism of colonic transit following the parasympathetic denervation in rats. J Surg Res 2011;171(2):
- 46 Gribovskaja-Rupp I, Takahashi T, Ridolfi T, Kosinski L, Ludwig K. Upregulation of mucosal 5-HT3 receptors is involved in restoration of colonic transit after pelvic nerve transection. Neurogastroenterol Motil 2012;24(5):472-478, e218
- 47 Itagaki R, Koda K, Yamazaki M, et al. Serotonin (5-HT3) receptor antagonists for the reduction of symptoms of low anterior resection syndrome. Clin Exp Gastroenterol 2014;7:47-52
- 48 Wexner SD, Coller JA, Devroede G, et al. Sacral nerve stimulation for fecal incontinence: results of a 120-patient prospective multicenter study. Ann Surg 2010;251(3):441-449
- Mellgren A, Wexner SD, Coller JA, et al; SNS Study Group. Longterm efficacy and safety of sacral nerve stimulation for fecal incontinence. Dis Colon Rectum 2011;54(9):1065-1075
- 50 Devroede G, Giese C, Wexner SD, et al; SNS Study Group. Quality of life is markedly improved in patients with fecal incontinence after sacral nerve stimulation. Female Pelvic Med Reconstr Surg 2012; 18(2):103-112
- 51 Chiarioni G, Salandini L, Whitehead WE, Biofeedback benefits only patients with outlet dysfunction, not patients with isolated slow transit constipation. Gastroenterology 2005;129(1):86-97
- 52 Byrne CM, Solomon MJ, Young JM, Rex J, Merlino CL. Biofeedback for fecal incontinence: short-term outcomes of 513 consecutive patients and predictors of successful treatment. Dis Colon Rectum 2007;50(4):417-427
- 53 Ho YH, Chiang JM, Tan M, Low JY. Biofeedback therapy for excessive stool frequency and incontinence following anterior resection or total colectomy. Dis Colon Rectum 1996;39(11):1289-1292
- 54 Kim KH, Yu CS, Yoon YS, Yoon SN, Lim SB, Kim JC. Effectiveness of biofeedback therapy in the treatment of anterior resection syndrome after rectal cancer surgery. Dis Colon Rectum 2011;54(9):
- 55 Bartlett L, Sloots K, Nowak M, Ho YH. Biofeedback therapy for symptoms of bowel dysfunction following surgery for colorectal cancer. Tech Coloproctol 2011;15(3):319-326